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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,424	06/21/2001	Karl Kavalkovich	640100-426	4226

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EXAMINER

NAFF, DAVID M

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 09/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/831,424

Applicant(s)

KAVALKOVICH ET AL.

Examiner

David M. Naff

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): 35 U.S.C. 112, first paragraph.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

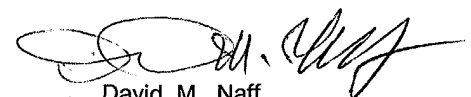
Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: _____

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____



David M. Naff
Primary Examiner
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ATTACHMENT TO FORM PTOL-303

In traversing the 35 U.S.C. 112, second paragraph rejection, applicants urge that the meaning of "contacting the cells with a chondroinductive agent" would have been understood readily by those skilled in the art in view of the specification. However, claims 12 and 18 do not recite "contacting the cells", but instead recite "cells are contacted". The claims are not being rejected because the meaning of "chondroinductive agent" is not understood, but because the claims are unclear as to when the cells are contacted with the agent. Claim 12 is unclear as to whether the chondroinductive agent is part of the composition, or the claim is reciting a step that occurs before or after the composition is formed. If the claims are requiring contacting the agent with the gel layer containing the cells as in Example 1, then claim 12 should be in product-by-process form since requiring cells contacted with the agent is requiring a process step. Claim 18, to be clear and definite, should similarly require a process step of contacting the agent with the gel layer containing the cells. The claims, not the specification, define metes and bounds of the invention, and the claims, per se, must be clear and definite as to boundary lines of the claimed invention.

Applicants' arguments traversing the 35 U.S.C. 103 rejections are unpersuasive for reasons in the previous office action of 5/20/03 and for reasons that follow.

As to claim 23 requiring *in vitro* cartilage formation, this would have been obvious from Pittenger et al disclosing *in vitro*

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chondrogenesis with mesenchymal stem cells in contact with a chondroinductive agent. There is nothing seen to lead one to believe that having the cells in a gel as disclosed by Grande et al or Borland et al would prevent *in vitro* culturing of the cells to form cartilage.

5 While Pittenger et al does not form an alginate gel, gel formation is disclosed by Grande et al, and also by Borland et al when applied. The references are applied in combination and must be considered together as a whole rather than each alone. The use of a gel containing cells rather than a cell pellet as disclosed by
10 Pittenger et al is taught by Grande et al, as well as by Borland et al when applied, and it is clear that chondrogenesis can occur without using a cell pellet. There is nothing in Pittenger et al to lead one to believe that the functioning of a chondroinductive agent requires the use of a cell pellet. Showing an improvement over Pittenger et al
15 fails to make the present invention unobvious since the rejection is not based on using the procedure of Pittenger et al, but on using the procedure of Grande et al or Borland et al when modified by using a chondroinductive agent as suggested by Pittenger et al. Using a chondroinductive agent when culturing mesenchymal stem cells to produce
20 cartilage is obviously going to produce an improvement. Even if the hyaluronic acid of Pittenger et al is produced by the cells cultured to produce cartilage, Pittenger et al suggest that hyaluronic acid is a chondroinductive agent, and its use for this function as in claim 15 in contact with the mesenchymal stem cells would have been obvious
25 since TGF- β 3 is used by Pittenger et al in contact with the stem cells.

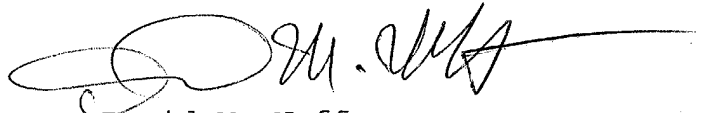
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It is granted that Borland et al does not use a condroinductive agent and hyaluronic acid as the agent. However, using a condroinductive agent and hyaluronic acid as the agent is suggested by Pittenger et al. As noted above, the references are applied together,
5 and must be considered in combination as a whole.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 703-308-0520. The examiner can normally be reached on Monday-Friday 9:30-6:00.

10 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application is assigned is (703) 872-9306.

15 Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is 703-308-0196.



David M. Naff
Primary Examiner
Art Unit 1651

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DMN
9/10/03